

Trade

Eucortone

Mark

(CORTIN, A. & H.)

Extract of Adrenal Cortex

for the treatment of Addison's Disease
and Other Conditions

Highly Active Highly Purified

EUCORTONE is an extract of adrenal cortex prepared by Allen & Hanburys, Ltd. and biologically standardized on adrenalectomized animals. Remarkably successful results are obtained by the treatment of Addison's disease with it. In February, 1931, Allen & Hanburys were able to supply cortin-containing extract for treatment of cases, and their preparation proved effective also in the treatment of the more chronic phases of the disease.¹⁻⁶ Its purity and activity have been much improved since it was first introduced. It contains less than 0.01 per cent. of nitrogen and is practically free from adrenaline.

Medical Research Council Report

Eucortone and another preparation were used in an independent investigation into the actions of adrenal cortical extract in Addison's disease, and the results of this investigation were reported for the Medical Research Council. The series of cases numbered nine.

They were all clearly pigmented, though pigmentation is not always present in Addison's disease. Five of them were treated successfully and two with temporary success, and one of the others died from a different cause (auricular fibrillation), during a remission of the Addison's disease. Four of the five successfully-treated patients were acutely and severely ill at the beginning of the treatment, and had since been maintained with daily doses of 7.5 to 15 grm. of sodium chloride. The other was a chronic case of moderate severity. Receiving 5 c.cm. of **Eucortone** (equivalent to 2 c.cm. of the present **Eucortone**) intramuscularly every day for a week and then every other day, he improved very rapidly. He was discharged at the end of five weeks, no further treatment being given to him; and he maintained his improved state. The report advises divided daily dosage for intramuscular injections above 10 c.cm. (the equivalent of 4 c.cm. of the present **Eucortone**), but undivided daily doses for intravenous injection. It says that suprarenal (adrenal) cortical extracts are of very definite value in the treatment of Addison's disease if given in adequate dosage: symptoms of asthenia, muscular weakness, and digestive disorders (especially nausea, vomiting, and diarrhoea) are promptly relieved; the appetite returns, the weight increases, the mental outlook improves, and the pigmentation fades slowly—though it faded *rapidly* from the *mucous membranes* in the surviving patients; the blood-pressure may take two or three months to improve significantly; and then its improvement seems to depend on giving sodium chloride with or after the cortical extracts.

Eucortone in Marasmus

Experiments on rats, and pathological studies in patients, have shown that apparent inability to make use of food, and so to gain weight adequately, is among the results of adrenalectomy and is an important characteristic of marasmus; that negative metabolism of



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nitrogen and mineral salts is an outstanding feature of adrenal insufficiency and of marasmus; that chronic inanition, associated with lack of vitamin A or vitamin B₂ in the diet, or with secondary pellagra, may produce hypertrophy and congestion, atrophy, or insufficiency, of the adrenal glands; that marasmus may be produced by chronic infection and may also be associated with secondary infection; that, in acute infection and intoxication, the adrenals undergo changes varying from congestion and œdema to hæmorrhage and focal necrosis; and that, on the other hand, adrenalectomy diminishes resistance to toxins and drugs, whereas cortical extract may increase resistance to infection.

In a series* of five undernourished and wasted babies—unselected cases—the administration of **Eucortone** daily for varying periods, in what later seemed too small a dosage, was accompanied by a more rapid gain in weight than had been occurring in the previous two to twenty weeks during which these patients had been in hospital.

In a second series*, consisting of fourteen babies treated at the Baby Hospital, Kensington, the diagnosis of marasmus was confirmed as far as possible, and the patients were kept in hospital for about a fortnight, before **Eucortone** was given. Then **Eucortone** was injected intramuscularly in a dosage of 1 minim per 2 lb. of body-weight daily for not more than fourteen days; and, after a break of ten to fourteen days, the injections were resumed for six to ten weeks. The diet and the general supervision of the baby were, as far as possible, unaltered throughout; and each of the babies received a preparation containing vitamins A and D. Of the fourteen babies, eleven gained more in weight during the periods of treatment with **Eucortone** than during the previous periods; and, in a smaller degree,

they gained more than during the break between the first and second courses of **Eucortone**. Eight of these eleven continued to gain weight while they were still in hospital after the administration of **Eucortone** had ceased; and they all, though some of them to a less extent, continued to gain weight while they were under observation as out-patients.

The three patients besides the eleven just mentioned, in this series, were one suffering from otitis media, one who died without responding to the treatment, and one who left the hospital in an improved condition though without definitely responding to the treatment.

During the years 1930 to 1934 the annual numbers of deaths from marasmus at the hospital had ranged between seven out of fifteen, eleven out of nineteen, and ten out of sixteen cases admitted. From June, 1935, the date when the **Eucortone** treatment with adequate dosage began, this death-rate fell so much that, in 1936, only two out of the fourteen marasmic babies died.

Eucortone in Acute Toxæmia of Burns

A. Grollman⁹ says that, in uncomplicated cases of superficial burns, characteristic changes take place in the adrenals, which become swollen and deep red, with extensive hæmorrhages visible on section and with the cells pale, swollen, and in process of hydropic degeneration.

W. N. Kemp¹⁰ says the marked pathological changes found in the adrenal cortices suggest that acute cortico-adrenal insufficiency, secondary to these changes, plays a prominent part in deaths from burns. He suggests that generous administration of cortin would prevent an otherwise inevitable death from that cause.

In three cases²¹ of very severe established toxæmia resulting from burns, the administration of **Eucortone** was followed by recovery. Death within a short time could have been predicted in two of the cases with almost complete certainty. The investigators had not known recovery from these conditions under any methods of treatment previously used; and with every confidence they attributed the recovery in these cases to the administration of **Eucortone**. How the preparation acted was not clear, but it seemed to increase the efficiency of the circulatory mechanism. The investigators advise that the extract should be considered as an adjuvant, not as a substitute for established treatment, in acute toxæmia of burns and also, perhaps, as future trial might show, in "**secondary shock**" (**circulatory collapse**). They regard as essential the use of local and general measures which have been designed especially to combat secondary shock and to minimize acute toxæmia and sepsis. In extensive and severe burns, they recommend continuous intravenous infusion of dextrose saline from an early stage, to mitigate injury to the liver cells. They advise that the following doses of **Eucortone** should be administered till a hundred hours after the injury, and renewed if toxic manifestations appear: for children, 1 c.cm. every two hours from the onset of acute toxæmia; for adults, 2 c.cm. or more every hour.

Cortin in Other Conditions

Successes have been reported from the use of adrenal cortical extract in various other conditions, including minor, hypo-adrenalism¹², neurasthenia¹³, progressive muscular dystrophy,^{14, 15} hyperthyroidism,^{16, 17} hyperemesis gravidarum,^{18, 22} psoriasis,^{23, 5} and infections.^{26, 27}

Method of Treatment

Eucortone is preferably administered by the intramuscular route, except in a crisis, when a more rapid

action is obtained by intravenous injection. In chronic cases, where the dose is relatively small, the subcutaneous route is adequate and more convenient.

To avoid the risk of symptoms of intolerance, it is important to give the injections slowly and to begin with a small dose—not more than 1 c.cm. If a preliminary injection of 1 c.cm. is not followed by unfavourable symptoms (*e.g.*, rise of temperature) within an hour, it may be considered quite safe to proceed with the treatment. It is advisable to increase the dosage gradually.

As in the case of insulin, the dosage suitable to each particular case must be found by trial. It is important that the dose should be large enough; and, if the patient shows no symptoms of intolerance, there is no risk of overdose.

The usual dosage in Addison's disease is from 4 to 8 c.cm. daily in divided doses; but a dose corresponding to as much as 8 c.cm. of the present Eucortone has been given at one time, and as little as 16 to 32 c.cm., spread over several days, can secure successful results in a crisis or in face of an impending crisis. In accordance with suggested practice,⁴ however, in a crisis, 20 c.cm. should be given on the first day and 8 c.cm. daily afterwards till there is a definite clinical improvement, then 4 c.cm. daily till the patient walks easily, and finally a maintenance dose of 2 c.cm. daily. The initial 20 c.cm. may be omitted when there is no immediate danger, and the dosage may begin with only 4 c.cm. a day in mild cases.

To eliminate discomfort from the injection of adrenal cortical extract, one writer²⁸ recommends the addition of 3 drops of 1-per-cent. procaine hydrochloride (without adrenaline) to the dose in the syringe, the last drop being allowed to fill the needle.

Authorities^{2, 29} emphasize the importance of combining the specific substitution-therapy with treatment

of dehydration, in the crises, by means of a solution of glucose (10 per cent.) and sodium chloride (1 per cent.). Loeb, Atchley, Gutman, and Jillson³⁰ gave 15 grm. of sodium chloride in a day with striking success, and Graham³¹ reported that Loeb had, by this method, succeeded in reducing the dosage of cortin in one case to one-fifth of the previous amount. Even more striking was the maintenance by 7.5 to 15 grm. of sodium chloride daily in the four severe cases successfully treated with adrenal cortical extract and reported² for the Medical Research Council (see pp. 1-2).

Leonard G. Rowntree and his associates²⁹ pointed out the need for abundant rest, warmth, relaxation, freedom from work and worry, protection from stresses and strains, and an adequate intake of foods and fluids.

Whole adrenal gland (e.g., 10 grains once to thrice daily) provides a valuable accessory means of treatment.

Price in Great Britain and Northern Ireland
(subject to alteration without notice):

Eucortone is supplied in india-rubber-capped bottles of 10 c.cm., at 20/- 25/-

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